

DIAGNOSIS OF THE ETIOLOGICAL  
FACTORS IN FEMALE STERILITY\*

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DIAGNOSTIC study of sterility nowadays implies the clinical investigation of husband and wife and includes consideration of all genital factors as well as constitutional factors which may have an etiological bearing on the fruitless wedlock. This seems a far cry from the first decade of the present century when it was common practice to consider only the female in deciding the question of childlessness. The patient was subjected to routine bimanual examination which was as likely as not to include inspection of the vagina and the cervix, and perhaps occasional exploration with a uterine sound. The decision of sterility or fertility was based upon such routine gynecological examination which sought mainly to exclude gross abnormalities. It is no wonder that the prognosis was as often wrong as right.

The past twenty years have witnessed considerable progress in this field. First in chronological importance was the growing recognition that the male partner may be and often is responsible for the failure to conceive. This notion became better established as a fact through the work of Huhner who devised his biologic compatibility test. Thus arose the idea of a sterile mating in contradistinction to the sterile mate. So important did this concept appear to us that a Huhner test was resorted to before proceeding with detailed examination of the status of the female.

The second step was the determination, by a clinical test, of patency of the upper portion of the female genital tract, namely the fallopian tubes, thus obviating the necessity of resorting to laparotomy for that purpose. Incidentally the patency of the cervical canal and uterine cavity was also ascertained. The method paved the way for biochemical and biodynamic research in the field of sterility.

The third step was the recognition of the importance of the constitu-

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tion of each of the married partners.

The fourth step was the development of our knowledge of hormones. The pioneers and workers who have made noteworthy contributions in this field are too well-known to be dwelt upon in this presentation.

Present day investigation of a sterile couple involves procedures that have come into practice in the last twenty years and has become a highly specialized chapter in gynecology, urology and general medicine. It calls for teamwork and correlation of studies undertaken in the various fields of medicine and biology. Some of the etiological factors are precise and reliable, others are not so reliable; some leave no doubt as to the factual data obtained, while others yield data whose interpretation leaves much doubt. In some directions we may have gone far afield and subjected the couple to unnecessary and useless procedures. In the present paper an attempt has been made to evaluate and appraise the etiological factors as well as the diagnostic procedures employed.

The causes of female sterility may be said to be local and general and they may also be considered as of major or minor importance. Of the local causes the more common are mechanical as opposed to functional. The latter are bound up with disturbances of the endocrine and nervous systems and with certain constitutional conditions. The mechanical causes are obstructive, due to anatomical dislocations, or for the most part pathological alterations of the genital apparatus. According to S. W. Meaker who analyzed seventy-five sterile marriages from this viewpoint, the constitutional factors play almost an equal role of importance with local genital factors. The local factors were found by Meaker in the proportion of 4 to 3 of the constitutional factors. In the experience of different observers the proportion may vary but in any event the constitutional factors will be found to play an important role in sterility.

Amongst the constitutional factors are chronic infections of the tonsils and sinuses with their systemic effects; thyroid dysfunction; syphilis; protein starvation; vitamin deficiency; alcoholism; and diabetes. Lead poisoning is a systemic condition which I have 'occasionally encountered in the husband. Hypertension, in my experience, has appeared to exert more of a deleterious result upon an existing pregnancy than upon the ability to conceive. These patients are predisposed to habitual abortion.

The causative factors of sterility, as Meaker has repeatedly pointed

out, are apt to be multiple. The local factors in the female outweigh similar factors in the male. According to Meaker the ratio is 4 to 1, whereas the constitutional factors are about even. I have not had occasion to check the relative incidence of these factors but there can be no doubt of the importance of the constitutional status in all cases and in many cases to a decisive degree.

Although an absolute cause of sterility as azospermia or ablated tubes may at once be established, it may in many instances be considered worthwhile to determine associated factors in order to decide the important question whether corrective procedures should be undertaken at all.

Unless something can be done about restoring spermatogenesis for example or tubal patency it would seem idle at first sight to proceed with any further exploration of the other factors. Nevertheless, it is only by most careful analysis of the constitutional condition, including associated circumstances that the possibility of restoration of function can be accomplished. Moreover, the normal mate may wish to achieve a child by remarriage. The request may be made for artificial insemination using the fertile semen of a known or unknown donor. If neither of these alternatives is chosen, the couple may wish to submit to a complete investigation with the end in view of adopting a child in case there is no hope for offspring of their own.

An individual of a markedly diminished fertility mating with another of more or less the same lowered fertility will be unlikely to be fruitful. If cross mating in the human family were possible, we should be in possession of data that would prove exceedingly helpful. This limitation in our knowledge prevents us from properly advising individuals whose keen desire for offspring prompts them to seek divorce in order to remarry. Obviously we cannot give such individuals assurance that the second marriage will prove fruitful. The potential fertility or sterility of the mate can only be proven by coital relations.

In the majority of instances there is more than one fault in both partners. Theoretically, by correcting one or several in the one or other mate, fertility should be enhanced; the deficiency of the one being compensated by the adequacy of the other.

The threshold of fertility varies not only with different individuals but in the same individual at different times. In women there is the absolute prepubertal sterility except in rare cases of precocious sex de-

velopment; there is further the relative sterility of lactation and its final establishment in the menopause. Relative infertility undoubtedly occurs in the same individual at various phases of the menstrual cycle. There are a few human comparisons with the famous bull (Sybil Gamboges) who could serve three different cows every day of the year and fertilize all of them. In the human sphere there is no doubt that the one individual enjoying a higher degree of fertility compensates for the relatively lowered fertility of the other partner.

Estimating the degree of fertility is obviously difficult. One cannot speak of it in mathematical terms. The highest degree of fertility may be seen in a married couple where the first exposure results in pregnancy and where conception follows every first time they choose to have another child, only one sex act being necessary to be fruitful. Each mate of this hypothetical fertile couple may be assumed, all other factors being equal, to be fruitful in another marriage with a partner enjoying equally high fertility or relatively diminished fertility. On the other hand, despite complete absence of detectable barriers, some couples remain childless for years although every artificial aid has been employed.

The evaluation of these factors is difficult except in a few categories. They may be said to have major or minor importance. Some are obvious while others are difficult to estimate, e.g., gynaplasia, azospermia, tubal occlusion, impotence, are factors of major importance that are quickly discovered. Minor factors are not so obvious, yet they may at times assume major importance as, for example, when it is accidentally discovered that douching invariably follows the sex act because the patient believes she must cleanse herself promptly. Effluvium seminis may similarly defeat attempts at fertilization especially when the amount of semen is primarily deficient.

The deterrent factors are recognizable in about 90 per cent of cases of sterility. This does not mean, however, that the faults are all amenable to corrective measures. Nor does restoration to the normal average necessarily assure fertility. Until we learn more about the chemistry of reproduction we shall probably not be able to explain why many married couples remain infertile despite the fact that they have only minor faults or no appreciable stigmata. This fact should make us pause in prognosticating the chances of success for any proposed therapeutic measure.

As in all clinical diagnosis, a comprehensive medical history is ex-

tremely useful. This includes reference to impregnation in marital or extramarital relations; the termination of the pregnancies and character of the puerpera or abortions. Thirty-five per cent of 307 patients in my series who gave a history of artificial abortion proved to have tubal closure; an additional 22 per cent showed impaired patency. A history of gonorrheal infection is significant, as is the history of other infectious diseases especially mumps. In the female the effect upon the gonads of this infection is not as clearly manifest as in the male but that it exerts a harmful influence upon the ovaries is highly probable. Appendicitis has undoubted etiological importance in the female especially where pelvic peritonitis has occurred. Tubal occlusion and impaired patency were found by uterotubal insufflation in over half of 487 women complaining of sterility who gave a history of appendectomy. More specific is the record of pelvic inflammation and so-called abdominal influenza. Urinary symptoms especially right after marriage are suggestive of a Neisserian infection even when this is not affirmed by the patient. It has been shown to be the precursor in a number of cases of sterility due to tubal occlusion. Details of sex life with reference to libido, orgasm and habit; frigidity and dyspareunia are also of interest. It is amazing at times to what extent ignorance of sex hygiene on the part of otherwise intelligent individuals shrouds the sex act. Contraceptive methods undoubtedly affect fertility for longer or shorter periods after their use has been stopped. The duration of involuntary sterility is also of interest in relation to the general question as to how much time should be considered adequate to stamp a marriage sterile or infertile. The onset of menstruation, its character in adolescence, after marriage and after pregnancies, its duration, all in careful detail are of particular importance. Amenorrhea, oligo- and opsomenorrhea are very frequently associated with infertility. Not only is the number of theoretical ovulations reduced under these circumstances but the depressed menses indicate abnormal ovarian function and depressed constitutional states. Effluvium seminis is perhaps not as important a factor as was formerly claimed for it, but in some cases it may assume major importance.

Only a few remarks with reference to the Huhner test which has become more or less the special task of the gynecologist.

The finding of ample numbers of motile spermatozoa with good morphologic characteristics pretty nearly exonerates the male from being responsible for the infertility. It is the best evidence of his potency—

mechanical and generative. With this finding no further examination of the semen is necessary and one can proceed to inquire into the other factors involved in the infertile female.

If, however, the cervical and vaginal smears show few or no spermatozoa, examination of an unmixed semen becomes necessary. If the latter shows evidence of normal production as to amount of secretion, numbers of spermatozoa and with respect to their morphological characteristics, one may conclude that there was some interference with proper intromission or, what is less common, the semen was expelled from the vagina immediately after ejaculation. Detailed inquiry into the sex act usually discloses the fault in one or the other or both partners.

If, on the other hand, there is an abundance of spermatozoa in the vaginal secretion, most of which are dead, and none or a few are to be found in the cervix, it is evidence that the vaginal secretions are hostile, thus affording little or no opportunity for the spermatozoa to reach the cervical canal. It is rare to find abundant numbers of normally motile spermatozoa in the vagina and none in the cervix.

Without going too far into this inquiry one may say that the more copious the seminal ejaculate with its proportionate sperm content the more likely is conception to take place. Semen deficient in amount and in sperm content is less likely to be fruitful, all other factors being equal. The hazards confronting the spermatozoa in the lower portion of the genital tract require a surfeit to make up for the losses. A common mistake is to state that it takes but one spermatozoon to impregnate the ovum. One spermatozoon sent on its way from its source would stand one chance in two or three hundred million of reaching the goal.

In the physical examination search is made for conditions especially that interfere with the sex act, with the proper reception of semen, with factors that would be hostile to spermatozoa and impede their ascent to the tubes where they ultimately meet the ovum. Such deterrents may be seen in malformations and deformities; in the presence of infection of the urethra, vagina, Bartholin glands and cervix. Though spermatozoa can retain their motility in pus, the associated dyspareunia, secondary effects upon the male as well as cervical blockade can interfere with sperm migration. Malpositions of the cervix may interfere with favorable reception of semen and sperm ascent. Ulcerations of the introitus and vagina, unless chronic, and these are rare, may be responsible for failure of consummating the sex act. Stenosis and endocervicitis are common

deterrents. Cervical hypoplasia is in itself no hindrance. The cause lies deeper and is traceable to possible ovarian hypofunction. Adherent retroversion and retroflexion are frequently associated with adherent and strictured fallopian tubes which are more responsible than the uterine dislocation. Movable retroversions and retroflexions are not essential deterrents. Uterotubal insufflation has proved valuable in estimating the etiological importance of the distorted uterine position. Adnexal masses especially when tender, and tenderness alone, are other easily demonstrable etiological factors. When non-tender adnexal masses are present, tubal insufflation may serve to differentiate between ovarian cysts and hydrosalpinges, patent tubes pointing to the former. Retention cysts of the ovaries and dermoids are the only palpable lesions which have practical significance in relation to sterility. Other disturbances referable to the ovaries which may bear upon the problem of sterility such as hypofunction due to small ovaries, failure of corpus luteum formation, cannot be determined by the bimanual examination. Normal ovaries are not invariably palpable and small atrophic ovaries escape palpation most frequently. Malignant tumors of the ovaries seldom enter into consideration in this connection. I do not recall a single instance where carcinoma of the ovaries was accidentally met with in a case coming for the relief of sterility.

Regarding the ovaries in general and ovulation in particular, only secondary and conjectural data are available. The assay of excretion of sodium pregnandiol as advocated by Brown and Venning which gave much promise at first was not proven completely reliable according to Hamblen. There is as yet no one test or correlated reliable tests or direct evidence of ovulation except during laparotomy when inspection of the tube contents can be made.

An idea of the ovarian influence on the tubes and indirectly also of the pituitary influence may be obtained by kymographic uterotubal insufflation. The tubal muscle which is always under the influence of estrogenic stimulation has been shown to exhibit, in experimental animals, an increasing number of rhythmic contractions per minute, the force and frequency of which are increased during ovulation. In the human female rhythmic contractions of varying frequency and amplitude can conveniently be recorded by uterotubal insufflation throughout the postmenstrual interval. Correlating the clinical observations with the work of Seckinger and Snyder on the extirpated surviving human

fallopian tubes, it may be said that the character of the contractions in general reflect the degree of estrogenic stimulation and function. In many cases when this test has been carried out during the mid-menstrual interval, the contraction force and frequency suggested hypermotility which may have been coincidental with ovulation.

This evidence added to that obtained by appropriate staining of routine vaginal smears as carried out by Papanicolaou and Schorr can give an idea of good or deficient estrogenic function. They cannot however be construed as positive diagnostic evidence of ovulation. Electro-potential determinations, temperature measurements and other biodynamic methods have so far not proven reliable nor have the painstaking bioassays of hormonal excretion established definite criteria for determining the exact date of ovulation of any menstrual cycle. It would prove very helpful were it possible in a sizable series of cases to correlate such bioassays and vaginal smears showing cyclic changes and tubographs obtained by peruterine insufflation with actual inspection of the tubes and recovery of the ova from them.

Regarding the endocervical secretion, the best evidence of its normality is the effect exerted upon the spermatozoa. If motile normally appearing spermatozoa can be recovered from the cervical canal, it is evidence that they have encountered a favorable environment. If non-motile spermatozoa are uniformly recovered from the cervical canal, although motility is demonstrable in the vaginal secretion, the cervical secretion may be said to be hostile. The nature of the hostility is not always determinable. The pH (hydrogen ion) value may be within physiological limits—pH 8.0, pH 9.0, the viscosity may be regarded as normal and the stained smear may show no specific changes. In other words, we are not in a position as yet to determine the nature of the lethal factor which the spermatozoa encounter in the cervical canal in any given case. It is not unlikely that there is some, as yet undetermined, substance in the serum or the mucus or the cellular content in the cervical secretion which paralyzes the motility of the spermatozoa, at least of that particular mate, preventing their ascent to the upper portions of the female genital tract. I have had occasion to examine the cervical secretion in the same woman after she had intercourse with several men and found the same relative hostility to the spermatozoa. Further work in immunology including the rH factor recently discovered may throw light on the antagonism of the cervical secretion which has proven the



burial ground for countless spermatozoa.

For practical purposes the physical examination of the uterus affords a clue to the normal or subnormal activity of the ovaries. A hypoplastic uterus usually bespeaks subnormal ovarian activity. A well-developed uterus indicates good ovarian function. If there is associated menstrual deficiency (oligomenorrhea, opsomenorrhea) with a hypoplastic uterus it is fairly presumptive evidence that the genital muscular tube is not receiving adequate estrogenic impulses. In my experience a rugous, short vaginal portion of the cervix with more or less quadrangular margins instead of the circular or elliptical margins is pathognomonic of infantilism. Such a vaginal portio has not developed completely and resembles the infant's portio vaginalis as I have had the opportunity of observing by the vaginal endoscope in several hundred cases.

The endometrium has telltale value with respect to the endocrine effect of the ovaries and anterior pituitary. But for this an examination of the uterine curettings is necessary. In the past ten years curettage has been replaced by the more convenient endometrial biopsy. The best time for taking an endometrial biopsy, if it is to be carried out once, is two or three days preceding the next ensuing menstrual period. If a pregravid endometrium is found, it is *strong presumptive evidence* that the ovulation-menstruation process is in order and that ovulation has been followed by corpus luteum formation. The endometrium has been prepared for the reception of an ovum. Whether this happens only in the presence of a fertilized ovum or regularly when the ovum is unimpregnated, as in the virginal state, has not been established. The absence of the predecidual or pregravid type of endometrium has been assumed to indicate that menstruation was not preceded by ovulation, in other words the bleeding is said to be anovulatory. On the other hand it must be remembered that the administration of estrogenic hormones followed by progesterone can produce in the menopause pregravid like changes in the endometrium. Furthermore, it has been found lately that stilbestrol alone can initiate the secretory type of endometrium in some cases during menopause.

Since practically all the investigations with endometrial biopsy have been carried on in married women, it is not possible to state in how many cases an ovum may have been impregnated and been blighted in its incipency thus producing no actual delay in the menstrual period. If it were possible to obtain a pregnancy reaction in its incipency, i.e.,

a day or two after impregnation instead of waiting till the next menstrual period has been delayed, it would help to clear up much of the question of ovular vs anovular menstruation. E. Novak has had the opportunity of studying the endometrium in girls with essentially normal menstruation and was convinced that it can occur from an endometrium of non-secretory type. This theory could possibly be further explored best by carrying out endometrial biopsy in a group of cases where the husband is definitely sterile and the wife faithful to her marriage vows.

An inherent limitation of endometrial biopsy, as of bioassays of hormones, is the fact that its data indicate what has taken place the particular month in which it was done. The findings of one month do not hold for the next or any other month. The same criticism holds true for hormonal assays as well as for vaginal smears. Endometrial biopsy has the disadvantage of possibly interfering with a very young pregnancy which is lamentable in the case of the infertile woman. For this reason it should be undertaken only when abstinence has been maintained during that particular menstrual cycle.

Dysmenorrhea is not infrequently associated with sterility. The underlying mechanism is not always clear. Although pregnancy does occur despite dysmenorrhea, which it cures frequently, the underlying factor may be part of the endocrine or other systemic disturbance which is responsible. The true explanation is not at hand and the theories advanced are for the most part speculative.

*Tests for tubal patency.* The tubal factor is one which lends itself to satisfactory evaluation because of kymographic uterotubal insufflation on the one hand and of hysterosalpingography on the other. By studying a large series of cases of sterility with both methods we are in a good position to appraise the etiologic role played by tubal obstruction. In a questionnaire which was answered by 259 gynecologists upon the results of 40,387 insufflations, tubal obstruction was found in 11,728 cases (about 28 per cent). In my own series of 3,380 cases of sterility tubal obstruction was met with in 984, an incidence of 29.1 per cent. There were an additional 16.77 per cent (567 patients) who had adherent tubes and 11.75 per cent (397 cases) who had strictured tubes. In well over half the cases there was evidence of tubal pathology which can be accorded etiological importance to preclude conception or to interfere with impregnation. I have employed radiopaque solution in a

relatively small series of cases because I have found it possible to diagnose all the important data relative to tubal patency or obstruction by means of uterotubal insufflation.

My first efforts in 1914, as those of William Cary, who was the first in this country to report upon intrauterine collargol injection, were directed toward x-ray visualization of the tubal lumina. I have preferred tubal insufflation with CO<sub>2</sub> gas to hystero-graphy since 1925 when a kymograph was added to the insufflating apparatus for the following reasons: It is more convenient. Its results are immediate while, for patency to be diagnosed by radiopaque substances, one or two days must be awaited in many instances. Uterotubal insufflation enables us within a few minutes to distinguish graphically *uterotubal spasm, tubal strictures and the physiological activity of the tubal muscle*—conditions not readily determinable by means of hystero-graphy. Furthermore, CO<sub>2</sub> because of its prompt resorption leaves no residue in the tubes or in the pelvis, as does iodized oil, which induces foreign body granulomata, thus producing total blockage where permeable strictures had previously existed. I have observed a considerable number of women who have become totally sterile although they had the possibility of conceiving before iodized oil was injected into the uterus.

The impression is extant that by means of iodized oil one can distinguish unilateral from bilateral permeability. This is a mistake because the tube which is not visualized roentgenologically may be in a condition of spasm or it may be comparatively more hypertonic than the other tube. The hypertonic tube may also have a narrower lumen which offers greater resistance to the CO<sub>2</sub> gas. This resistance may require an increased pressure of a few millimeters of mercury in excess of that which permits the gas to be transmitted through the less spastic or more widely calibered tube. Randall has shown this to be the case with iodized oil and I have had occasion to observe the same phenomenon, i.e., on a subsequent examination an apparently closed tube became open while the open tube appeared closed.

Another advantageous claim made for hysterosalpingography is that it locates the exact point of obstruction. This can be arrived at for all practical purposes by carefully carrying out the procedure of uterotubal insufflation and paying attention to the pain reactions and distributions.

The value of x-ray opaque media in sterility lies in the fact that it enables us to demonstrate the configuration of the uterine cavity and

possibly visualize polypi and submucous myoma which may have etiological importance. But for this purpose, use of a viscous soluble crystalline iodine solution is superior as it leaves no permanent residue. Time does not permit description of the proper technique of uterotubal insufflation or of hystero-graphy. Recently I have resumed the use of a hysteroscope which gives promise of enabling us to explore the uterine cavity in a manner quite analogous to that of cystoscopy.

*Sterility viewed from the endocrinologic standpoint.* The gross disturbances of the endocrine system are too obvious to require description here. They are moreover relatively rare. Of far greater clinical importance in relation to sterility are the less marked disturbances, the intermediary types which the French have aptly called "*formes frustes*." They are however not easy to define. Practically everyone knows what are the primary and secondary sex characteristics of male and female. Gross abnormalities are easily recognized whether they be in the genitalia or in the general body architecture. But there are undoubtedly some individuals, it would be difficult to say how many, who are predestined to sterility, so to speak, by failure of development and defective germ plasm.

Although we have at hand hormonal assay methods that differentiate androgenic from estrogenic hormones, these methods have not as yet enabled us to define specifically the degree of "maleness" and "femaleness" or to interpret the significance of androgen-estrogen ratios as suggested by Koch and his group. So far they have shown that both hormones are excreted by each individual; so that biologically and hormonologically, as embryologically, we are all partly male and partly female. A cyclical variation of estrogenic production and excretion has been shown for normal females in studies that have required painstaking work (R. T. Frank, et al). Carried out on a larger scale such bioassays of estrogenic and androgenic substances may lead to more reliable criteria.

At present it is useful to bear in mind certain secondary sex characters which clinical observation and anthropometric studies have established to differentiate the two sexes. Considered in relation to each other and to the whole organism they give practical aid in estimating gonadal function. These secondary sex characters are divisible into two categories, the psychic or spiritual and the somatic. On the somatic side in the female there is the finer texture of the skin and the hidden superficial

veins, the full development of the breasts and absence of body hair with longer growth of the hair of the head, the triangular arrangement of the pubic hair as opposed to the masculine escutcheon reaching the umbilicus, and the absence of beard growth. The character of the voice and speech including the recession of Adam's apple are distinctly different from that of the male. The distribution of fat about the hips and fullness and roundness of the nates, the less sturdy muscular development, the narrower skeletal development of the shoulder girdle and wider pelvic girdle, the shortness of lower extremities compared to the trunk and the swaying motion of the hips are other female sex characters. The presence of the accessory organs of the genital apparatus, namely, small clitoris, normal vagina, well developed cervix and uterus considered in conjunction with the secondary sex characters already mentioned, betoken the presence of functioning ovaries whether these are palpable or not. On the psychic side is the preference of sexual approach to men, the maternal instinct, and other generally recognized psychic characteristics of women.

If, for example, the female presents typical secondary sex characters and gives a history of normally recurring menstrual flow without pain and shows normally developed genitalia, one may, for all practical purposes, assume that her ovaries are performing their endocrine function. Since the ovaries are controlled by the pituitary, the surmise also holds for normal functioning of this motivating endocrine gland. Of all the disorders of endocrine function which have direct influence over the genital sphere, those of the thyroid are appreciable and susceptible of determination in a practical way.

It has been recognized, chiefly through the observations of Litzenberg, that a depressed thyroid state is frequently associated with sterility. The menses may be scant or they may be excessive; usually the former. There is a tendency to weight increase. The basal metabolism may show a marked reduction. Thyroid medication with dietary and physical regimens can increase fertility in these individuals.

Determination of sugar tolerance and of blood cholesterol has some clinical and endocrine significance. Blood examination and urinalysis are necessary to determine the general state of health. Hormonal assays (estrogenic, androgenic and gonadotropic) have so far yielded interesting data. Upon these data have been based corrective measures, which consisted of the administration of endocrine products but unfortunately

they have not proven to have the hoped for therapeutic value. At present our most reliable hormone is thyroid.

In conclusion I wish to call attention to the tendency in some quarters of overdoing the investigation of sterility. The pendulum has seemed to swing too far away from the middle of the road. From the cursory casual fashion in which sterility was managed a generation ago, there is at present a plethora of procedures many of which are not only unnecessary in every case but also are fraught with suspense and anxiety on the part of the patient which lower her susceptibility to conceive by reducing her peace of mind and general well-being.

Many examples of excessive and uncritical investigation, leading to overzealous treatment with fruitless results as a consequence, might be cited but for the limited time at my present disposal.

Obviously, those procedures should be employed that have a definite purpose supported by practical experience. In general I would emphasize the following steps in the inquiry: (1) A complete medical history especially detailed in the sphere of genital function and the constitutional state. (2) General physical examination with particular reference to that of the genitals and secondary sex characters. (3) The Huhner test and if necessary examination of the unmixed semen. (4) Tubal patency test. (5) Urinalysis; blood examination including serologic tests for syphilis. (6) BMR determination and (7) in individual cases as the indications arise, further investigation by means of specialized tests including serological, hormonological, roentgenological and biochemical.

The clinical appraisal of the patient including her psychic peculiarities, domestic happiness, dietary habits and sex habits underlying her inability to conceive must continue to receive first consideration while laboratory methods judiciously applied as in other fields of medicine may serve as useful aids.